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FOUR REASONS WHY
FDA'S INITIATIVE IS IMPORTANT

1. Sea Change in FDA Attitude

FDA has previously sought to avoid any jurisdiction over tobacco under its present legal authority.

Dr. Kessler has shown a willingness to commit the Agency to regulate cigarettes, while preserving options to back away or defer to Congress.

2. Discarding of Legal Precedent

FDA has distinguished all prior FDA and court decisions about FDA's jurisdiction over tobacco and cigarettes as "fact-based." A different factual record could therefore lead to a different legal result.

3. Change of Political and Legal Dynamic

FDA has now said that it may already have jurisdiction over nicotine products. This removes major political burdens from Congress. Dr. Kessler has also set forth a roadmap that can be used by tobacco opponents long after he leaves FDA.

4. Flexibility in FDA Regulatory Approach: No Hobson's Choices

FDA's theory permits control of some tobacco products without requiring FDA to ban all tobacco products.

FDA's theory permits control of some tobacco products without appearing to "approve" other tobacco products.

FDA's theory permits focus on "higher risk" products rather than "lower risk" ones.

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Slide 2

FDA ROADMAP FOR CLASSIFYING NICOTINE AS A DRUG

Step 1. Find that nicotine at certain levels fulfills the statutory definition of "drug." This finding could be made through any of a variety of FDA procedures, from typical rulemaking to typical investigation and enforcement action.

Step 2. Declare nicotine used at those levels to fulfill the statutory definitions of "new drug" and "prescription drug."

Step 3. Find that products delivering those levels of nicotine (i.e., cigarettes) fulfill the statutory definitions of either "drug" or "device."

If products are "drugs" they are also "new drugs" and "prescription drugs."

If the products are "devices" they are also "Class III devices."

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FDA ROADMAP FOR CLASSIFYING NICOTINE AS A DRUG

Step 4. Require FDA approval of either

A "new drug application" ("NDA") for each "drug" product, or

A "premarket approval application" ("PMA") for each "device" product.

Step 5. Determine that no NDA or PMA contains adequate scientific data demonstrating the safety of the product or its effectiveness for a medical use.

Step 6. Advise Congress of FDA's conclusions.

Step 7. In the absence of special legislation by Congress to regulate tobacco products, commence enforcement actions to remove unapproved products from the market.

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FDA ROADMAP FOR CLASSIFYING NICOTINE AS A DRUG (ALTERNATIVE ROUTE)

Step 4. Commence enforcement (or other judicial) action without providing opportunity for submission of DNA or PMA.

Steps 1-3 could be undertaken without a rulemaking process through an internal investigation.

FDA would not have an administrative record.

FDA would probably rely on some "wrongdoing" or "fraud" in selecting its initial target for enforcement action.

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KEY STATUTORY DEFINITIONS

DRUG -- An article

"intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man . . . ," or

"intended to affect the structure or any function of the body of man . . ." (other than food).

Critical Concepts:

"Intended for use"

Alternative tests: "treat disease" or "affect body function"

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KEY STATUTORY DEFINITIONS

NEW DRUG -- "Any drug . . .

> the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof. . . ."

Critical Concepts

- Presumption of "newness"
- "General recognition among experts"
- Conditions of use in the labeling
- The "New Drug Application" (NDA)

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KEY STATUTORY DEFINITIONS

PRESCRIPTION DRUG -- Any drug which

is a habit-forming drug (limited definition); or

is not safe for use except under the supervision of a physician, because of its toxicity or other potential for harmful effect, the methods of its use, or the collateral measures necessary for its use; or

is limited by an approved NDA to use under physician supervision.

Critical Concepts

Unsafe for unsupervised use for its intended application

Restricted by FDA without findings (most "new drug" products start life as Rx, then go OTC later)

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KEY STATUTORY DEFINITIONS

DEVICE -- Any "instrument, apparatus, implement . . . or other similar or related article, including any component, part, or accessory, which is . . .

> "intended for use in the diagnosis of a disease or other condition, or in the cure, mitigation, treatment, or prevention of disease in man . . ."
>
> "intended to affect the structure or any function of the body of man . . ."

and "which does not achieve any of its principal intended purposes through chemical action within or on the body of man . . . and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes."

Critical Concepts

> Applies to "drug delivery systems"
>
> Novel devices are automatically placed in Class III (highest level of regulatory control) until reclassified. Class III devices may not be marketed without prior FDA approval of a "premarket approval application" (PMA)

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THE ESSENTIAL ISSUE: CAN FDA SHOW THAT NICOTINE IS A DRUG?

All of the consequences of NDA and PMA flow from the threshold determination that nicotine is a drug.

1. FDA must show either

   Nicotine is intended for use to treat, mitigate, cure, or prevent a disease, or

   Nicotine is intended for use to affect the function of the body.

   FDA does not have to prove both elements of the definition.

   Dr. Kessler has referred to both elements of the definition in recent statements. This creates ambiguity and increases FDA's options.

2. FDA must also show that this intent is that of the seller of nicotine-containing products.

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HOW WOULD FDA ATTEMPT TO SHOW THAT NICOTINE WAS USED TO AFFECT THE FUNCTION OF THE BODY, OR USED TO "TREAT" A DISEASE?

FDA has cited "accumulating evidence" that "the nicotine ingredient in cigarettes is a powerfully addictive agent. . . ."

Drug addiction or drug dependence generally is described as involving psychological and physiological changes in the body:

Euphoric effects -- pleasurable effects that reinforce repetition of use

Tolerance -- increasing amounts of drug are needed to produce the same pleasurable effects

Withdrawal effects -- physical discomfort or other physically impairing symptoms upon cessation of use

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FDA HAS ALREADY RECOGNIZED THAT NICOTINE USE -- AT CERTAIN LEVELS -- CAN LEAD TO WITHDRAWAL SYMPTOMS

Dr. Kessler referred to the recent research that "nicotine, when delivered by cigarettes, produces physiological dependence resulting in withdrawal symptoms when smokers are deprived of nicotine."

FDA has approved the nicotine patch and nicotine gum products as drugs for use to treat or prevent withdrawal symptoms in connection with a smoking cessation program.

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FDA WILL ATTEMPT TO SHOW THAT NICOTINE -- AT CERTAIN LEVELS -- IS USED TO AFFECT BODILY FUNCTION AND PREVENT WITHDRAWAL SYMPTOMS

FDA may argue that

> Smokers use cigarettes in the same way that nicotine patches and gum are used (to provide nicotine in order to treat "addiction" or to prevent "withdrawal symptoms" associated with smoking cessation)
>
> Smokers use nicotine for the purpose of affecting the function of their body. Dr. Kessler's letter says "cigarettes enjoy a market that is based . . . on the need of smokers to satisfy that addiction."

In the past, FDA has applied a broad definition of "disease" to include almost any impairment of bodily function.

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FDA DOES NOT HAVE TO PROVE THAT NICOTINE IS ADDICTING

FDA only has to show that smokers develop either a physiological or psychological dependence resulting in physical withdrawal symptoms on cessation of smoking.

On this basis, FDA could conclude that nicotine, delivered at or above certain levels, stimulates or satisfies that dependence or relieves or prevent withdrawal symptoms.

FDA has data from patch and gum research showing both the symptoms and the fact that controlled administration of nicotine relieves these symptoms.

To demonstrate an effect on bodily function, FDA must establish more than the fact that the article stimulates the senses or alters the body chemistry.

The product must have a specific physiological effect on the particular bodily function or body structure.

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FDA DOES NOT HAVE TO PROVE WHAT LEVEL OF NICOTINE IS NOT ADDICTIVE

FDA has only to show that when consumed at or above certain levels, nicotine stimulates or satisfies the dependence or relieves or prevents withdrawal symptoms.

FDA has traditionally focused attention on clear and noncontestable levels of risk to establish tolerances or upper limits, then progressively lowered the limits over time as new data develop.

This approach means that FDA does not have to find that nicotine (or a cigarette) is "safe" at some level. Rather, FDA may assert that nicotine-containing products that deliver levels of nicotine below the level that is clearly "addicting" are not subject to FDA's jurisdiction as "drugs."

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CAN FDA SHOW THAT NICOTINE IS INTENDED FOR DRUG USE?

A product is a drug because of its intended use, which may or may not be the same as its actual use or its ability to achieve the intended use.

- Honey and tea have been held to be "drugs" when promoted to treat or prevent various diseases.

In identifying a product's intended use, FDA looks at the manufacturer's or seller's intent.

- FDA not bound by the seller's subjective claims, that is, what is explicitly stated on the label.
- FDA can find intent based on objective evidence of the seller's intent. Objective evidence can be derived from "any relevant source" including nonpromotional materials and strictly internal company documents.
  - FDA has relied on SEC filings, sales or marketing strategy memoranda, patent claims, and instructions to sales representatives.
  - Evidence admitted in product liability litigation can be used by FDA to establish intent.

FDA may also impute an intent to a seller.

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ARGUMENTS FDA MIGHT USE TO SHOW OBJECTIVE INTENT OF CIGARETTE MANUFACTURERS

1. Cigarettes are made through processes that remove all the nicotine, then nicotine is added back to the final product.

   This argument appears in new Coalition petition.

2. Nicotine is added to cigarettes by "spiking" to supplement what is present in natural tobacco leaf.

   Dr. Kessler has expressed FDA's "understanding that manufacturers commonly add nicotine to cigarettes to deliver specific amounts of nicotine."

3. Manufacturers can produce cigarette brands or formulations with varying levels of nicotine content. The choice to continue to market those with high levels of nicotine is not dictated by technological limits.

   FDA's letter states: "Although technology was developed years ago to remove nicotine from cigarettes. . . , cigarettes are still marketed with levels of nicotine that are sufficient to produce and sustain addiction."

Is this OR?

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"BUT CONSUMERS PREFER PRODUCTS WITH HIGHER LEVELS OF NICOTINE"

The industry response in the past regarding the manufacturer's intent can be summarized:

The industry is supplying a product for "smoking pleasure."

Consumers decide which product attributes they prefer to provide this pleasure.

Consumer preferences are expressed through the market.

De-nicotinized and low nicotine formulations have limited popularity.

FDA may now attempt to use consumer choice and the industry's intent to meet consumer demands to impute an intent to the manufacturers.

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THE DOCTRINE OF ADOPTED OR IMPUTED INTENT

Some courts have suggested that a seller can be held to intend a nonlabeled use for its product if it is aware that customers use the product for that purpose.

> This language has been "theoretical" -- no case has actually found such adopted or imputed intent.

The court's have further suggested that intent may be imputed only where the evidence shows the product is used "almost exclusively" for the drug use and that the labeled use is in practice virtually nonexistent.

> This was basis for U.S. Court of Appeals upholding FDA's denial of the 1977 ASH petition to regulate cigarettes as drugs.

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FDA MAY ATTEMPT TO SHOW THAT THE VAST MAJORITY OF USERS OF HIGH NICOTINE CIGARETTES DO SO FOR A DRUG EFFECT

FDA's letter states:

> Cigarettes enjoy a market that is based in part on the need of smokers to satisfy [their] addiction.
>
> A Canadian survey suggests that 80 percent of smokers believe they are addicted to cigarettes. Other data suggest that a comparable percentage of smokers are, in fact, addicted.
>
> Research has revealed that 77 percent of smokers desire to quit but cannot primarily because of nicotine addiction.

FDA may claim that these smokers use high nicotine products to affect the function of their bodies ("sustain their addiction") or to avoid withdrawal symptoms from smoking cessation ("treating addiction" and "preventing or mitigating disease symptoms").

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OTHER ARGUMENTS FDA MIGHT USE TO DEMONSTRATE ADOPTION OF DRUG INTENT ON PART OF CIGARETTE MANUFACTURERS

1. Consumer perception and preference research by manufacturers could indicate awareness of smokers' intended use.

   FDA may focus on long-term users of high nicotine products and their reactions to low nicotine products.

2. Manufacturers may have studied the pharmacological and behavioral effects of nicotine and decided it is "addicting."

3. Manufacturers may be aware of the FDA approval and clinical use of nicotine patches and gum products.

NOTE: FDA may seeking evidence bearing on these questions by visiting manufacturers, by interviewing current and former employees, and by interactions with plaintiffs' lawyers and antismoking advocates.

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IMPLICATIONS OF THE FDA INITIATIVE: CONGRESS

FDA may collaborate with Congress to effect passage of legislation giving FDA defined and tobaccco-specific jurisdiction, in lieu of asserting drug jurisdiction.

Congress may prefer to let FDA proceed under existing law, rather than be called on to vote on tobacco-related issues.

Congress may proceed in parallel with an FDA investigation, and act legislatively after a better record exists.

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IMPLICATIONS OF THE FDA INITIATIVE: FDA INVESTIGATIONS

FDA appears to be aggressively seeking information relevant to the issues outlined above.

FDA inquiries may

place burdens on firms,

disrupt coordination among industry, and

keep industry off balance.

FDA may seek to assert jurisdiction through inspection authority, warrants or other procedural issues.

FDA has access to materials not available to the tobacco industry, such as the clinical and preclinical research on nicotine patches and gum.

FDA may (willingly or unwillingly) provide information obtained to Congress and through Congress to plaintiffs' bar and antismoking advocates.

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IMPLICATIONS OF THE FDA INITIATIVE: NICOTINE SCIENCE

Industry should become familiar with addiction terminology and research generally, as well as the studies bearing specifically on alleged nicotine dependence and withdrawal symptoms.

Needed to rebut FDA in general.

Needed to address issue of what level of nicotine ingestion is necessary to present "withdrawal symptoms."

Needed to identify what levels of nicotine in cigarettes FDA may permit.

Industry should review its research on physiological effects of nicotine on humans.

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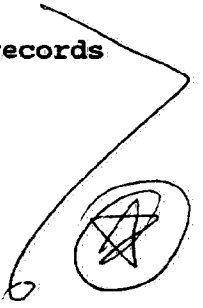
IMPLICATIONS OF THE FDA INITIATIVE: CONSUMER INTENT

Industry should determine what exists in its own records bearing on the issue of why people smoke:

- Consumer response to low nicotine and de-nicotinized products
- Consumer complaints or inquiries
- Company-sponsored research



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IMPLICATIONS OF THE FDA INITIATIVE: MANUFACTURING

Industry should be prepared to explain fully the manufacturing processes by which nicotine levels are controlled and why (if so) any nicotine is added to that contained in leaf tobacco.

Industry should consider the impact of FDA's approach on the development of new products and new technologies for controlling nicotine levels.